

ABSTRACT

This invention provides fragments of HCV NS3 helicase, and crystalline compositions thereof, based on subdomains of HCV helicase protein. The protein fragments 5 are stable, soluble, and structurally sound. They can be expressed at high levels in conventional expressions systems, such as *E. coli*, to permit efficient, large-scale production for NMR-based screening applications and production of [<sup>2</sup>H, <sup>13</sup>C, <sup>15</sup>N]- and [<sup>13</sup>C, <sup>15</sup>N]-labeled polypeptides for structural NMR studies. Helicase fragments of the present invention are useful in the most advanced NMR techniques available, *e.g.*, NMR-based drug discovery 10 techniques such as SAR-by-NMR, in biological assays to discover inhibitors of HCV NS3 helicase, and to evaluate the mechanism of action and substrates for HCV NS3 helicase. Crystals of the present invention are useful for structure-based drug design studies using x-ray crystallographic techniques.